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10/530,171

05/17/2005

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EXAMINER

BRISTOL, LYNN ANNE

ART UNIT

PAPER NUMBER

1643

MAIL DATE

DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/530,171

Applicant(s)

HIRAKAWA ET AL.

Examiner

Lynn Bristol

Art Unit

1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 27 June 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,3,4 and 12-41 is/are pending in the application.
- 4a) Of the above claim(s) 12-41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3 and 4 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. Claims 1, 3, 4 and 12-41 are all the pending claims for this application.
2. Claims 2 and 5-11 were cancelled, new Claims 36-41 have been added and Claims 1, 3, 4, 18, 19, and 31-33 have been amended in the Response of 6/27/07. The amendment of Claim 1 incorporates the subject matter of cancelled Claims 2 and 10, and the amendment of Claims 3 and 4 incorporates the subject matter of cancelled Claim 2.
3. Claims 12-41 are withdrawn. It is noted that new Claims 36-41 are drawn to a method but depend from cancelled Claim 3 of the elected group for an antigen under examination. Thus it is not clear what the intended claim scope is for new Claims 36-41 or from what other pending-withdrawn method claim(s) they should depend.
4. Claims 1, 3 and 4 are all the pending claims under examination.
5. Applicants amendments to the claims have necessitated new grounds for rejection. This action is FINAL.

### **Withdrawal of Objections**

#### ***Specification***

6. The objection to the improper use of the trademark e.g., Vectastain Elite ABC, is withdrawn in view of the amendment to the specification on pp. 2-3 of the Response and further in view of Applicant's comments on p. 8 and 9 of the Response.

***Claim Objections***

7. The objection to Claim 10 for the recitation "in the Sequence Listing" is withdrawn and moot in view of the cancelled claim. Applicants' comments on p. 10 of the Response are acknowledged.

**Withdrawal of Rejections**

***Claims - 35 USC § 101***

8. The rejection of Claims 1-9 under 35 U.S.C. 101 as being drawn to non-statutory subject matter for any antigen exposed on a cell surface at the formation of a tumor mass, which reads on the antigen per se which is found in nature, is withdrawn. Claims 2 and 5-9 are cancelled and Claims 1, 3 and 4 have been amended to recite that the antigen is "isolated". Applicants' comments on p. 10 of the Response are acknowledged.

***Claims - 35 USC § 112, second paragraph***

9. The rejection of dependent Claims 2 and 5-11 as being indefinite for the recitation "at the formation of a tumor mass" in claim 1 is withdrawn and moot in view of the cancelled claims.

10. The rejection of Claims 3 and 4 in lacking antecedent basis for the recitation "the solid tumor" is withdrawn in view of amended Claim 1 to recite "a solid tumor." Applicants' comments on p. 10 of the Response are acknowledged.

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11. The rejection of Claims 3 and 4 as being indefinite for the relationship between the amount of antigen being measured on the solid tumor and the cultured solid tumor cell is withdrawn in view of the amended claims. Both claims are amended to recite that the cell comprising the solid tumor is formed by subcutaneous transplantation of the cultured cell, and the amount of expressed antigen is compared between the tumor cell of the solid tumor versus the cultured cell. Applicants' comments on p. 10 of the Response are acknowledged.

12. The rejection of Claims 3 and 4 as being indefinite for the recitation "the existing amount" is withdrawn in view of the amendment to delete the phrase. Applicants' comments on p. 11 of the Response are acknowledged.

13. The rejection of Claim 4 in lacking antecedent basis for the recitation "the cell surface" is withdrawn in view of the amended claim to recite "on the surface of a cell of the solid tumor". Applicants' comments on p. 11 of the Response are acknowledged.

14. The rejection of Claim 10 for the recitation that residues 600-1,960 of SEQ ID NO: 17 comprise the N-terminal domain is withdrawn and moot in view of the cancelled claim. Applicants' comments on p. 11 of the Response are acknowledged.

***Claims - 35 USC § 112, first paragraph***

***Written Description***

15. The rejection of Claims 5-9 under 35 U.S.C. 112, first paragraph, in lacking written description support for the genii of mutant proteins for a cytoskeleton protein (Claim 5), a myosin protein (Claim 6), and a non-muscular myosin heavy chain type A protein (Claims 7-9) is withdrawn and moot in view of the cancelled claims. Applicants' comments on p. 11 of the Response are acknowledged.

***Enablement***

16. The rejection of Claims 5-9 under 35 U.S.C. 112, first paragraph, in lacking enablement for any mutant of a cytoskeletal protein, a myosin protein and a NMMHC IIA protein which is antigenic, partly exposed on the cell surface and at the formation of a tumor mass is withdrawn and moot in view of the cancelled claims. Applicants' comments on p. 11 of the Response are acknowledged.

However, in view of Applicants amendment of Claims 1, 3 and 4 to incorporate the subject matter of cancelled Claim 10 for residues 600-1,960 of SEQ ID NO: 17 (C-terminus of the non-muscle myosin heavy chain A protein), the amendment raises new grounds for rejection as discussed below.

***Claim Rejections - 35 USC § 102***

17. The rejection of Claims 1 and 5-11 under 35 U.S.C. 102(b) as being anticipated by Chiavegato et al. (Virchows Archiv. 426:77-86 (1995); cited on the PTO-form 892 of 1/11/07) is withdrawn and moot for cancelled Claims 5-11 and withdrawn for Claim 1 in view of the amendment to recite that the tumor cell is derived from a transplanted cultured tumor cell. Applicants' allegations on p. 11 of the Response are acknowledged.

18. The rejection of Claims 1-4 under 35 U.S.C. 102(b) as being anticipated by EP 399257 A1 (Oregon Health Sci. U.; published 11/28/90; cited in the IDS of 4/27/05) is withdrawn and moot for cancelled Claim 2 and withdrawn for Claim 1 (and Claims 3 and 4) in view of the amendment to recite that the tumor cell is derived from a transplanted cultured tumor cell, and the antigen comprises residues 600-1,960 of SEQ ID NO: 17. Applicants' allegations on p. 11 of the Response are acknowledged.

19. The rejection of Claims 1 and 5-11 under 35 U.S.C. 102(b) as being anticipated by WO 01/75067 (HYSEQ, INC; published 10/11/2001; cited in the IDS of 12/21/05) as evidenced by Saez et al. (PNAS 87:1164-1168 (1990); cited in the IDS of 12/21/05) is withdrawn and moot for cancelled Claims 5-11 and withdrawn for Claim 1 in view of the amendment to recite that the tumor cell is derived from a transplanted cultured tumor cell. Applicants' allegations on p. 11 of the Response are acknowledged.

**Rejections Maintained**

***Claims - 35 USC § 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

20. The rejection of Claims 1, 3 and 4 as being indefinite for the recitation "a cell positioned at the formation of a solid tumor" is maintained for reasons or record and as set forth below.

Applicants allege one of skill in the art would understand that the cell is positioned at the formation of the tumor.

Figure 2 and the figure legend for Figure 2 in the specification is the only description of the histological evidence showing the distribution of the non-muscle myosin heavy chain A (nmMHC-A) antigen (SEQ ID NO: 17) in what appears to be transplanted recombinant nmMHC-A-expressing cell lines, designated FL1, FL2 and FL7, and derived from HCT-15 (human colon cancer cell line). It is not clear from the evidence where with respect to the general histology, the formation of the tumor is occurring and where the cell should be positioned vis-à-vis this formation. Does this include the cells along the edge of a growing tumor mass, or cells associated with the vasculature or blood vessels found in a tumor, or cells breaking away from the solid tumor to form metastases, etc.? Would every cell in the solid tumor mass be expected to express a part of the antigen on its cell surface?

Clarification of the description of the histology is requested for the record.



**New Grounds for Rejection**

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

***Written Description***

21. Claims 1, 3 and 4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 3 and 4 are drawn to the antigen, a non-muscle myosin heavy chain type A (nmMHC-A) comprising residues 600-1,960 of SEQ ID NO: 17, and part of which is exposed on the surface of a cancer cell positioned at the formation of a solid tumor where the solid tumor is formed by subcutaneous transplantation of a cultured cancer cell.

The claims encompass any kind of cultured cancer cell and the solid tumor from which it is formed, and which express a part of the antigen on the cell surface comprising residues 600-1,960 of SEQ ID NO: 17.

The specification supports the following cultured cancer cells that show increased cell surface expression of nmMHC-A (SEQ ID NO: 17) when transplanted into an animal:

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Example 1: MKN45 gastric cancer cell line;

Example 2: recombinant nmMHC-A-expressing cell lines, designated FL1, FL2 and FL7, and derived from HCT-15 (human colon cancer cell line); and

Example 4: human colon cancer (Caco-2, DLD-1, SW620, WiDr-Tc, SW837), human esophageal cancer (TE-8), human gastric cancer (HSC-3, MKN-1, MKN45, B37). Notably, the cancer cell lines found to express a part of the nmMHC-A antigen (SEQ ID NO: 17) on the cell surface are gastric related in origin.

The specification does not demonstrate that the antigen comprising *only* residues 600-1,960 of SEQ ID NO: 17 would be the part of the antigen that is exposed on the cell surface of the cultured cell much less the transplanted cell positioned at tumor formation. Further, it is not expected that the recited domain (residues 600-1,960 of SEQ ID NO: 17) would even be able to associate with the cell membrane.

Wei et al. (Molec. Biol. Cell 11:3617-3627 (2000)) disclose a truncated nmMHC-A comprising residues 593-1961 and compare the intracellular localization of the protein with the full length protein in transfected HeLa cells. Wei teaches that the truncated protein has lost the ability to bind actin, but otherwise retains the property of filament assembly and the ability to be incorporated into endogenous myosin. In other words, the truncated protein is never shown to become associated with the cell membrane where it is exposed on the surface. Wei does not support truncated forms of nmMHC-A occurring on the surface of the HeLa cancer cell line. Wei teaches that despite the abnormal, rounded morphology of cells transfected with truncated nmMHC-A, the HeLa cells are capable of undergoing cytokinesis.

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One skilled in the art would reasonably conclude from the disclosure in the specification and the prior art, that a protein having only residues 600-1,960 of SEQ ID NO: 17, would be expressed on the surface of a cultured cancer cell much less increased in its expression for the transplanted cell. One skilled in the art would also reasonably conclude that not all cultured cancer cells express the full length antigen of SEQ ID NO: 17 on their surface, but that some cancer cells express the full length antigen of SEQ ID NO: 17 comprising residues 600-1,960 and which upon transplantation is increased in amount of expression.

### ***Conclusion***

22. No claims are allowed.

23. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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